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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/646,436	08/21/2003	Martin Gleave	UBC.P-030	9171

57381 7590 01/22/2009

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EXAMINER	
CHONG, KIMBERLY	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
01/22/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/646,436	GLEAVE ET AL.	
	Examiner	Art Unit	
	KIMBERLY CHONG	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2008 and 28 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,10,11,14,20,23 and 29* is/are pending in the application.

4a) Of the above claim(s) *20,23 and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,10,11 and 14* is/are rejected.

7)☐ Claim(s) ____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/28/2008 has been entered.

Status of Application/Amendment/Claims

Applicant's response filed 05/02/208 has been considered. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. With entry of the amendment filed on 05/02/2008, claims 1, 4, 10, 11, 14, 20, 23 and 29 are pending in the application. Claims 1, 4, 10, 11 and 14 are currently under examination and claims 20, 23 and 29 are withdrawn as being drawn to a non-elected invention

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4 and 14 depend from canceled claims and therefore fail to point out and distinctly claim the subject matter of the invention. Claims 4 and 14 will not be further treated on the merits because the subject matter of the claims cannot be determined without assumption regarding the limitations in the canceled claims.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional applications upon which priority is claimed fail to provide adequate support under 35 U.S.C. 112 for claims 10 and 11 of this application.

The claims are drawn to a pharmaceutical composition comprising a RNA molecule having a length of less than 49 bases and comprising a sequence as defined by SEQ ID No. 10.

The provisional applications 60/405,193, 60/408,152 and 60/472,387 disclose an RNA molecule 21 to 23 nucleotides in length. The above-mentioned applications fail to provide adequate support for RNA molecules less than 49 nucleotides in range but greater than 23 and further the applications fail to provide support for an RNA molecule less 21 nucleotides in length. If applicant feels there is adequate support then applicant must point out, with particularity, where such support can be found.

Therefore, claims 10 an 11 are accorded a priority date of 08/21/2003, the filing date of the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miyake et al. (Clinical Cancer Research 2000 cited on Applicant's IDS filed 03/31/2004), Tuschl et al. (US 2004/0259247), Fosnaugh et al. (US 2003/0143732) and Hammond et al. (Nature Reviews 2001, Vol. 2; pages 110-119).

The instant claims embrace dsRNA and are drawn to a RNA molecule having a sequence effective to mediate degradation or block translation of mRNA of a target gene wherein the target gene encodes a clusterin gene and the RNA molecule comprises a sequence as defined by SEQ ID No. 10 and further drawn to pharmaceutical compositions comprising said RNA molecule together with a pharmaceutically acceptable carrier.

Miyake et al. teach antisense oligonucleotides targeted to clusterin target gene TRPM-2, wherein the antisense oligonucleotide is capable of mediating degradation or blocking translation of the mRNA (see page 1655). Miyake et al. teach prostate cancer

is a commonly diagnosed malignancy and TRPM-2 has been found to be unregulated in prostate cancer and acts to inhibit apoptosis of said prostate cancer cells (see abstract and page 1655) and inhibition of TRPM-2 gene using antisense oligonucleotides provides a therapeutic treatment for prostate cancer (see page 1659-1662). Miyake et al. further teach screening active antisense oligonucleotides sequences targeted to the human TRPM-2 gene (see page 1659) and specifically identifies an antisense compound as AS ODN#2 which targets the human TRPM-2 translation initiation site as being capable of reducing TRPM-2 expression (see page 1659) which is the target site targeted by the claimed SEQ ID No. 10 sequence.

At the time of filing of the instant invention, it was well known in the art that RNAi using siRNA was becoming a more efficient method of silencing gene expression. Hammond et al. discusses siRNA and previous methods of reducing using inhibitory molecules such as antisense compounds and states that siRNA is a more potent method of silencing gene expression, requiring only a few molecules of siRNA per cell to silence gene expression (see page 110).

Tuschl et al. teach making and using siRNA for mediating gene silencing (see Example 1 and the siRNA User Guide beginning at paragraph 0178) and has demonstrated siRNA mediated silencing in mammalian cells and states that the use of short siRNAs holds great promise for Inactivation of gene function in human tissues and the development of gene-specific therapeutics (see paragraphs 0144-0151).

Fosnaugh et al. describes making siRNA reagents useful for modulating gene expression. Fosnaugh et al. teach identification of siRNA targets sites in any RNA

sequence by screening the mRNA transcript using a computer folding algorithm and describes siRNA that target a gene from a database, such as Genbank (see Example 2). Fosnaugh et al. teach using target sites that are known or have been determined as effective based on studies with other nucleic acid molecules such as antisense can be used to design siRNA as well as target sites known to be associated with disease or conditions such as those containing mutations or deletions (see Example 2). In Example 3, Fosnaugh et al. details selection of siRNA target sites in RNA and screening of siRNA to access activity and teach optimal parameters in designing said siRNA, such as having a GC content preferably 40-60% and comprising 2 nucleotide overhangs. Fosnaugh et al. teach the siRNA molecules are comprised of two strands which are 18 to 24 nucleotides in length (see paragraph 0122) or can be a hairpin structure (see paragraph 0057) and further comprises nucleotide overhangs (see paragraph 0058). Fosnaugh et al. teach the siRNA can be expressed from expression vectors comprising various promoters such as pol III promoters and termination signals (see paragraph 0220-0223).

It would have been obvious to one of skill in the art at the time the invention was made to use the methods taught by Tuschl et al. and Fosnaugh et al. to make a siRNA targeted to a clusterin/TRPM-2 mRNA for the silencing of gene expression.

One of ordinary skill in the art would have been expected to be able to design any siRNA targeted to any mRNA transcript because Fosnaugh et al. details the steps to effectively find a target site in any RNA and design and test siRNA molecules for specific RNAi activity. Fosnaugh et al. teach known target sites that have previously

been targeted by antisense compounds are useful as well as known target sites that have been shown in art to be responsible for certain disease and given Miyake et al. identifies an optimal target region, a region of TRPM-2 gene that is targeted by the claimed SEQ ID No. 10, one of ordinary skill in the art would have been expected to make the claimed RNA molecule comprising SEQ ID No. 10. Moreover, the claimed SEQ ID No. 10 would meet the design requirements as taught by Fosnaugh et al. and Tuschl et al. as discussed above and therefore one of ordinary skill in the art would have designed an RNA molecule targeted to TRPM-2 as taught by Miyake et al.

Both Hammond et al. and Tuschl et al. teach that it was well recognized in the art that siRNA was a more efficient method of silencing gene expression, requiring concentrations far less than the methods of the prior art, such as antisense compounds. In looking to reduce gene expression of TRPM-2, one of ordinary skill in the art would have wanted use the most efficient method to silencing gene expression and would have looked to the teachings of Tuschl et al. and Fosnaugh et al. for generation of siRNAs targeted to of TRPM-2 mRNA. Tuschl et al. and Fosnaugh et al. teach that production of siRNAs to any target gene is a matter of routine experimentation and optimization and clearly set forth the guidelines to design such molecules.

Finally, one of ordinary skill in the art would have expected to be able to generate a siRNA targeted to a TRPM-2 gene given Tuschl et al. and Fosnaugh et al. teach the basic steps to identifying any target site and making and screening siRNA molecules for activity, steps that are routine to one of ordinary skill in the art.

Thus in the absence of evidence to the contrary, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Kimberly Chong/
Examiner
Art Unit 1635